Amendments to the Specification:

Please amend the specification as shown:

Please delete paragraph [54] on page 24, and replace it with the following paragraph:

[54] Figure 1 (Panels A-E) illustrates various mutations identified in a heterologous negative stranded RNA virus that can be incorporated into recombinant HPIV2 candidates of the invention to yield attenuation or other desired phenotypic changes. Partial amino acid sequence alignments **(SEQ ID NOS 1-16, respectively in order of appearance)** are provided between HPIV2 wild-type (wt), HPIV3 wt, HPIV1 wt, or BPIV3 wt for regions of the indicated protein that contain known attenuating mutations. Based on these and similar comparisons, mutations are identified in a heterologous PIV or non-PIV virus for transfer into a recombinant HPIV2 of the invention. The amino acid position and substitution previously shown to confer a phenotypic change in the heterologous virus is indicated above each sequence alignment and wild type assignment is in bold font in the sequence alignment. The corresponding amino acid position in HPIV2 is indicated after the HPIV2 sequence. Amino acid positions that are conserved between all species of L protein in the alignment are underlined, representing additional targets for mutagenesis.

Please delete paragraph [55] on pages 24 and 25, and replace it with the following paragraph:

[55] Figure 2 illustrates modification of HPIV2 for use as a vector of other viral antigens. Panel A: Diagram (not to scale) of the HPIV2 genome illustrating the placement of a unique promoter-proximal *Not* I restriction site. The location of HPIV2/V94 nts 56-160 in the complete genome diagram is indicated with a box, and the sequence is shown above **(SEQ ID NO: 17)**. The sequence was modified from wild–type to contain a *Not* I restriction site (GCGGCCGC) one nucleotide prior to the translational start codon of the HPIV2 N gene (ATG, HPIV2/V94 nts 158-160). The *Not* I site was introduced by changing the HPIV2 sequence AGGTTCAA (HPIV2/V94 nts 149-156) to GCGGCCGC (*Not* I recognition sequence). The position of two potential N gene-start signals is indicated as shaded areas. The promoter element (open box) is a sequence that has been demonstrated to be important for viral replication and transcription in other Paramyxoviruses. Panel B: Insertion of the HPIV1 HN or RSV (subgroup A) G open reading frame as a supernumerary gene in the *Not* I site **(SEQ ID NOS 18, 19, 17, 18, 20, and 17, respectively in order of appearance)**. A gene–start, intergenic, and gene–end sequence identical to that found between the HPIV2 N and P genes (HPIV2/V94 nts 1909-1938) is inserted after each supernumerary ORF. These signals serve to terminate

transcription of the foreign ORF and start transcription of the downstream HPIV2 N gene, respectively. Each supernumerary gene cassette will be generated using PCR with a sense oligo that will include a *Not* I restriction site and an antisense oligo that contains gene-end (GE) and gene-start (GS) sequences that will be used to terminate transcription for the inserted gene and promote transcription for the HPIV2 N gene, respectively. A unique *BstE*II site is also included which will allow for the optional insertion of a second supernumerary ORF. The entire sequence is modified as necessary to conform to the rule of six by adjusting the length (n) of the sequence in the positions indicated by the arrow. The bottom section for each virus details the sequence of the HPIV2 backbone where the ORFs are to be inserted. This strategy can be used to engineer other unique restriction sites at any one of the gene junctions to allow for the insertion of multiple foreign genes.

Please delete paragraph [59] on page 26, and replace it with the following paragraph:

[59] Figure 6 provides a comparison of selected regions of the nucleotide sequence of the HPIV2 Toshiba and Greer strains **(SEQ ID NOS 21-40, respectively in order of appearance)**. The Toshiba and Greer sequences were aligned using the BESTFIT alignment program (Wisconsin Package Version 10.2, Genetics Computer Group (GCG), Madison, Wisconsin). Missing nts are indicated by (.). Ten regions were identified (A-J) that likely represent sequence errors in the reported Toshiba strain sequence. These sequences (antigenomic sense) are found in (A), the Toshiba strain N gene start signal sequence missing 1-nt, (B) the Toshiba strain N ORF, missing codon-195 (Arg), (C) the Toshiba strain N gene end (containing 1 extra nt) and P gene start signals (missing 1-nt), (D) P ORF (missing 1 nt), (E) P ORF (containing 1 extra nt) resulting in missense of P aa 316-319 (changes GSDM **(SEQ ID NO: 67)** to QVIL **(SEQ ID NO: 68)**), (F) HN 3' NCR (missing 1 nt), (G) L ORF (missing codon-378 (Ala)), (H) L ORF (missing codon-741 (Pro)), (I-J) L ORF (containing 3 extra nts, resulting in missense of L polymerase aa 1735-1743 (changing TLTKFDLSL **(SEQ ID NO: 69)** to NSNKVRFIPF **(SEQ ID NO: 70)**).

Please delete paragraph [60] on pages 26 and 27, and replace it with the following paragraph:

[60] Figure 7 illustrates the structure of nucleotide inserts used to make HPIV2 antigenomic cDNAs that do not conform to the rule of six. Panel A. The wt nt sequence **(SEQ ID NO: 41)** around the EcoRV restriction site near the end of the L ORF is shown. Panel B. The sequences of the six antigenomic-sense oligonucleotides **(SEQ ID NO: 42-47, respectively in order of appearance)** inserted at the EcoRV restriction site spanning HPIV2 nt 15554-15559 is shown. Oligonucleotide duplexes were inserted between nt

15556 and 15557. Each oligonucleotide duplex contains a silent ATC to *att* mutation that destroys the EcoRV site and recreates the last 11 codons of the L ORF, and 12 HPIV2 nt including the TGA stop codon (bold) followed by 0-5 additional nt. The designation of the recombinant viruses generated from the cDNAs is indicated to the left: the virus designated rHPIV2N94(+6) corresponds to the rule of six, while the others contain the indicated number of additional nt (+1 to +5). The length of each oligonucleotide insert is shown on the right, with the rule of six length and the total length of the antigenomic cDNA indicated in parenthesis.

Please delete paragraph [61] on page 27, and replace it with the following paragraph:

[61] Figure 8 illustrates nucleotide insertions and deletions detected in the genomic RNA of recombinant HPIV2s derived from cDNAs that do not conform to the rule of six (sequences are in antigenomic sense). Panel A. Four recombinant viruses were produced from cDNAs that did not conform to the rule of six, rHPIV2N94(+3), rHPIV2/V94(+4) **(SEQ ID NO: 50)**, r_AHPIV2/V94(+5) **(SEQ ID NO: 51)**, and r_BHPIV2N94(+5) **(SEQ ID NO: 52)**, contained nt insertions that resulted in a polyhexameric genome length. Two insertions containing a total of 3 nt were identified in the HN 5' and 3' noncoding regions (5' NCR **(SEQ ID NO: 48)** and 3' NCR **(SEQ ID NO: 49)**) of rHPIV2N94(+3). A 2-nt insertion within the intergenic (IG) region between the HN and L genes was identified in rHPIV2N94(+4). A 1-nt insertion was found in each clone of r_AHPIV2/V94(+5) and r_BHPIV2N94(+5), in one case at the end of the HN GE signal and in the other in the HN 3' NCR. Panel B. Two recombinant viruses produced from cDNAs that did not conform to the rule of six, rHPIV2/V94(+2) **(SEQ ID NO: 53)** and rHPIV2N94(+1) **(SEQ ID NO: 56)**, contained nt deletions that resulted in a polyhexameric genome length. rHPIV2N94(+2) was found to have a 2-nt deletion (underlined) within the IG region between the HN and L genes. rHPIV2N94(+1) was found to have a 1-nt deletion (underlined) near the end of the L polymerase ORF **(SEQ ID NO: 54)**. This resulted in a frame shift in the L coding sequence that deleted the last 13 amino acids **(SEQ ID NO: 55)** of L and replaced them with an unrelated sequence of 21 amino acids **(SEQ ID NO: 57)**, as shown. The nt sequence (antigenomic sense) in the region of the insertions is shown. The inserted nt are shown and the site of insertion is indicated by an arrow pointing downward. Deleted nt are shown and the location of the deletion is indicated by an arrow pointing upward. The HN 5' or 3' non-coding region (NCR), transcription gene end (GE) and gene-start (GS) (in bold type) and intergenic regions (IG) between the HPIV2 HN and L ORFs are indicated. The L polymerase translation initiation codon

(ATG) and translation termination codon (TGA) are underlined. The single letter amino acid designation is shown below the nt sequence for the wt and a mutant version of the HPIV2 L polymerase.

Please delete paragraph [62] on page 27, and replace it with the following paragraph:

[62] Figures 9A-F provide a nucleotide sequence for the HPIV2/V94 strain **(SEQ ID NO: 58)**.

Please delete paragraph [63] on page 27, and replace it with the following paragraph:

[63] Figures 10A-F provide a nucleotide sequence for the HPIV2/V98 strain **(SEQ ID NO: 59)**.

Please delete paragraph [64] on page 28, and replace it with the following paragraph:

[64] Figures 11A-F provide a nucleotide sequence for the HPIV2 Greer strain **(SEQ ID NO: 60)**.

Please delete paragraph [67] on pages 28 and 29, and replace it with the following paragraph:

[67] Figure 14 illustrates modification of a recombinant HPIV1 of the invention for use as a vector for heterologous protective antigens of different PIV and non-PIV pathogens according to the invention. Panel A provides a diagram of the HPIV1 genome that has been modified from wild-type to contain an Mlu I restriction site one nucleotide prior to the translational start codon of the N protein (starting at HPIV1 nt 113), or a Not I restriction site between the P and M ORFs, within the P gene 3' non-coding region (starting at HPIV1 nt 3609). Gene-start and gene-stop signals for each HPIV1 gene are shaded in gray and black, respectively. In panel B, the area enclosed by the rectangle around the Mlu I site is expanded and illustrates the insertion of the HMPV strain CAN83 F protein ORF (the complete F ORF is 1620 nt in length and encodes a 539 aa polypeptide. The length of the entire inserted supernumerary gene unit sequence is 1656 nt). For the recombinant virus that is illustrated in panel B, rHPIV1-F_{83}, the top sequence shows the insert that is generated using PCR with a sense oligo that includes an Mlu I restriction site **(SEQ ID NO: 69)** and an antisense oligo **(SEQ ID NO: 62)** that contains gene-stop and gene-start sequences that are used to terminate transcription for the inserted gene and promote transcription for the N gene, respectively. Additional nucleotides (indicated by R6) are inserted where necessary to conform the entire inserted sequence to the rule of six, and to maintain the HPIV1 gene start signal sequence phasing (Kolakofsky et al., J. Virol. 72: 891-899, 1998, incorporated herein by reference). The bottom section in the panel details the sequence of the HPIV1 backbone where the ORF is inserted **(SEQ ID NO: 63)**. The

naturally occurring gene-start sequence is boxed. The promoter element is a sequence that has been demonstrated to be important for viral replication and transcription. In panel C, the area enclosed by the rectangle around the Not I site is expanded and illustrates the insertion of the HMPV CAN83 strain G protein ORF from the CAN83 strain of HMPV (the complete G ORF is 660 nt in length and encodes a 179 aa polypeptide. The length of the entire inserted supernumerary gene unit sequence is 702 nt). For the recombinant virus that is illustrated in panel C, rHPIV1-G_{83}, the top sequence shows the insert that is generated using PCR with a sense oligo **(SEQ ID NO: 64)** that includes a Not I restriction site, gene-stop and gene-start sequences that are used to terminate transcription for the upstream P gene and promote transcription for the inserted supernumerary gene unit, respectively, and an antisense oligo that contains a NotI site **(SEQ ID NO: 65)**. Additional nucleotides (indicated by R6) are inserted where necessary to conform the entire inserted sequence to the rule of six, and to maintain the HPIV1 gene start signal sequence phasing. The bottom section in the panel details the sequence of the HPIV1 backbone at the P-M junction where the ORF is inserted **(SEQ ID NO: 66)**. The naturally occurring gene-end and gene start sequences are boxed. This strategy can be used to engineer other unique restriction sites at any one of the gene junctions or 3' or 5' portions of the genome or antigenome to allow for the insertion of foreign genes, as desired.